Test Type: CHRONIC Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE

CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Final #2/Rats

C Number: C93020D

Lock Date: 03/14/2003

Cage Range: ALL

Date Range: ALL

Reasons For Removal: ALL

Removal Date Range: ALL

Treatment Groups: Include ALL

Date Report Reqsted: 08/08/2005

Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

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CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

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FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG
Disposition Summary				
Animals Initially in Study	50	50	50	50
Early Deaths Moribund Sacrifice	18	12	10	23
Natural Death	12	8	8	10
Survivors	22	22	00	47
Terminal Sacrifice Animals Examined Microscopically	20 50	30 50	32 50	17 50
ALIMENTARY SYSTEM				
Intestine Large, Cecum	(50)	(50)	(50)	(49)
Ulcer	1 [2.0]	0.50.51	4 [0.0]	0.00.01
Edema Hemorrhage	1 [3.0]	2 [2.5]	4 [2.8] 1 [2.0]	2 [3.0]
Intestine Large, Colon	(50)	(50)	(50)	(50)
Inflammation, Chronic Active		1 [3.0]		
Intestine Small, Duodenum	(49)	(49)	(49)	(49)
Epithelium, Hyperplasia	(=a)	1 [3.0]	2 [3.0]	1 [2.0]
Liver	(50)	(50)	(50)	(50)
Angiectasis Clear Cell Focus	2 [1.5] 16	2 [3.0] 11	1 [2.0] 14	1 [3.0] 8
Mixed Cell Focus	4	6	6	o 4
Basophilic Focus	14	14	22	9
Hepatodiaphragmatic Nodule	5	5	7	8
Eosinophilic Focus	6	2	7	4
Degeneration, Cystic	3 [2.0]	5 [2.0]	4 [2.3]	
Necrosis, Focal		1 [2.0]	1 [3.0]	
Infiltration Cellular, Mixed Cell		2 [2.0]	4 [2.0]	
Regeneration Hemorrhage		1 [2.0]	1 [3.0] 2 [2.5]	1 [2.0]
Metaplasia, Atypical			ک [ک.ی]	1 [2.0] 1 [3.0]
Cyst				1 [3.0]
Bile Duct, Hyperplasia	33 [1.6]	36 [2.1]	31 [1.7]	17 [1.7]
Centrilobular, Necrosis	4 [2.0]	3 [2.0]	2 [2.0]	
Hepatocyte, Vacuolization Cytoplasmic	6 [3.2]	6 [3.3]	7 [3.3]	1 [3.0]
Kupffer Cell, Pigmentation		2 [2.5]		

a - Number of animals examined microscopically at site and number of animals with lesion b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE

CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Mesentery	(9)	(9)	(12)	(6)	
Accessory Spleen	l l	` ,	, ,	` ,	
Fat, Necrosis	7 [2.7]	6 [3.2]	8 [2.8]	3 [2.7]	
Pancreas	(50)	(50)	(50)	(50)	
Atrophy	18 [1 [.] 9]	28 [2.2]	32 [1.9]	21 [2.3]	
Cyst	2 [3.0]	3 [3.0]	5 [3.0]	3 [3.0]	
Hemorrhage			1 [3.0]		
Acinus, Cytoplasmic Alteration		1 [3.0]	1 [3.0]	1 [3.0]	
Acinus, Hyperplasia, Focal	2 [2.0]	5 [2.2]	4 [2.0]		
Salivary Glands	(49)	(50)	(50)	(50)	
Atrophy	1 [2.0]	()	1 [3.0]	2 [2.0]	
Necrosis	. []		1 [2.0]	1 [2.0]	
Stomach, Forestomach	(50)	(50)	(50)	(49)	
Inflammation, Chronic	2 [2.5]	1 [2.0]	()	2 [3.0]	
Ulcer	7 [3.0]	6 [3.2]	6 [3.5]	2 [4.0]	
Erosion	1 [2.0]	1 [1.0]	1 [2.0]	= [0]	
Edema	3 [3.0]	3 [3.0]	5 [3.4]	2 [3.5]	
Perforation	1	0 [0.0]	1	_ [0.0]	
Diverticulum	•	1			
Epithelium, Hyperplasia	7 [2.9]	6 [3.3]	8 [2.5]	5 [2.2]	
Stomach, Glandular	(50)	(50)	(50)	(49)	
Inflammation, Chronic	1 [3.0]	1 [2.0]	(00)	(10)	
Erosion	7 [2.6]	6 [2.3]	3 [3.0]	3 [2.0]	
Ulcer	4 [2.8]	2 [2.5]	3 [2.3]	1 [2.0]	
Cyst	4 [Z.O]	1 [3.0]	1 [3.0]	1 [2.0]	
Edema		2 [3.0]	1 [3.0]		
Glands, Hyperplasia	2 [2.0]	2 [5.0]	1 [2.0]	1 [2.0]	
ARDIOVASCULAR SYSTEM					
Heart	(50)	(50)	(50)	(50)	
Cardiomyopathy	41 [2.1]	44 [2.3]	44 [2.4]	36 [1.7]	
Thrombosis	5 [3.0]	1 [4.0]	5 [3.4]		
Inflammation, Chronic		1 [3.0]	1 [3.0]		
NDOCRINE SYSTEM					
Adrenal Cortex	(50)	(49)	(50)	(50)	
Degeneration, Fatty	12 [2.2]	11 [1.8]	15 [2.2]	8 [2.0]	

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Test Type: CHRONIC

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE **CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

Time Report Regsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Hyperplasia, Diffuse	1 [3.0]				
Hyperplasia, Focal	8 [1.5]	8 [1.5]	5 [1.8]	5 [1.6]	
Accessory Adrenal Cortical Nodule	17 [3.0]	16 [3.0]	16 [3.0]	9 [3.0]	
Hypertrophy, Focal	3 [2.0]	2 [1.5]	7 [2.0]	3 [1.7]	
Adrenal Medulla	(50)	(48)	(50)	(50)	
Hyperplasia	7 [1.9]	9 [1.6]	16 [1.8]	3 [1.7]	
slets, Pancreatic	(50)	(50)	(50)	(50)	
Hyperplasia	2 [2.0]	,	,	,	
Parathyroid Gland	(49)	(48)	(49)	(48)	
Hyperplasia	, ,	1 [2.0]	, ,	, ,	
Hyperplasia, Focal				1 [2.0]	
Pituitary Gland	(50)	(50)	(50)	(50)	
Pars Distalis, Angiectasis	, ,	4 [2.3]	1 [3.0]	2 [2.5]	
Pars Distalis, Cyst	2 [3.0]	3 [3.0]	1 [3.0]	1 [3.0]	
Pars Distalis, Hyperplasia, Focal	3 [1.0]	7 [2.0]	7 [2.3]	5 [2.8]	
Pars Intermedia, Cyst		1 [3.0]	1 [3.0]	1 [3.0]	
Γhyroid Gland	(50)	(50)	(50)	(50)	
Ultimobranchial Cyst	1 [3.0]			2 [3.0]	
C-cell, Hyperplasia	8 [1.8]	12 [2.0]	3 [1.3]	3 [1.3]	
Follicle, Cyst	4 [3.0]	5 [3.0]	2 [3.0]	3 [3.0]	
Follicular Cell, Hyperplasia	3 [1.7]		1 [2.0]		

GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Granuloma Sperm				1 [2.0]
Preputial Gland	(50)	(50)	(50)	(50)
Inflammation, Chronic	18 [2.0]	26 [2.0]	17 [2.1]	9 [2.1]
Hyperplasia	2 [2.0]			1 [2.0]
Cyst		2 [3.0]	2 [3.0]	1 [3.0]
Prostate	(50)	(50)	(50)	(50)
Inflammation, Chronic	40 [2.4]	32 [2.3]	35 [2.4]	25 [2.0]
Epithelium, Hyperplasia	4 [1.8]	10 [1.5]	2 [1.5]	3 [1.7]
Testes	(50)	(50)	(50)	(50)
Germinal Epithelium, Atrophy	12 [2.0]	11 [2.1]	24 [2.3]	14 [2.6]

a - Number of animals examined microscopically at site and number of animals with lesion b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

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Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

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FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Interstitial Cell, Hyperplasia	6 [1.3]	6 [1.5]	8 [1.3]	8 [1.5]	
EMATOPOIETIC SYSTEM					
Bone Marrow	(50)	(50)	(50)	(50)	
Myelofibrosis	2 [2.0]	1 [3.0]	,	,	
Hyperplasia	3 [2.7]	7 [2.9]	3 [3.0]	1 [2.0]	
Infiltration Cellular, Histiocyte	- [-···]	. []	1 [3.0]	1 [4.0]	
Lymph Node	(18)	(14)	(16)	(13)	
Mediastinal, Ectasia	3 [3.0]	1 [3.0]	1 [4.0]	(10)	
Mediastinal, Hemorrhage	2 [3.5]	1 [2.0]	4 [2.5]	6 [2.8]	
Mediastinal, Hyperplasia, Lymphoid	2 [3.5] 7 [2.9]	5 [2.6]	4 [2.5] 5 [3.2]	7 [2.4]	
Mediastinal, Hyperplasia, Lymphold Mediastinal, Pigmentation		ວ [∠.ບ] ວ ເວ ວາ		/ [∠. 4] 2 [2 2]	
	2 [2.0]	3 [2.3]	5 [2.6]	3 [2.3]	
Pancreatic, Ectasia	0.14.01		1 [4.0]	0.10.51	
Pancreatic, Hemorrhage	2 [4.0]	4 [0.0]	2 [2.0]	2 [2.5]	
Pancreatic, Hyperplasia, Lymphoid	4 (0.01	1 [2.0]	2 [3.0]	0.10.01	
Pancreatic, Pigmentation	1 [3.0]	1 [2.0]		3 [2.0]	
Lymph Node, Mandibular	(0)	(1)	(4)	(1)	
Ectasia			2 [3.0]		
Hemorrhage				1 [1.0]	
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)	
Hemorrhage	10 [1.8]	3 [1.3]	11 [1.5]	6 [1.5]	
Hyperplasia, Lymphoid	18 [2.2]	15 [2.2]	20 [2.1]	15 [2.1]	
Ectasia	3 [2.3]	5 [2.8]	3 [2.3]	1 [2.0]	
Pigmentation	15 [2.0]	8 [2.1]	16 [2.0]	12 [2.0]	
Spleen	(50)	(50)	(50)	(50)	
Hematopoietic Cell Proliferation	10 [1.8]	9 [2.0]	11 [2.1]	4 [1.8]	
Pigmentation	9 [2.9]	5 [2.8]	6 [2.3]	25 [2.6]	
Fibrosis	2 [2.5]	3 [3.0]	2 [3.0]	2 [2.5]	
Necrosis	2 [3.5]	1 [3.0]	1 [4.0]	1 [3.0]	
Hemorrhage	2 [0.0]	1 [4.0]	. []	. [0.0]	
Lymphoid Follicle, Atrophy	1 [3.0]	. []	1 [3.0]	2 [2.0]	
Lymphoid Follicle, Hyperplasia	1 [0.0]	1 [3.0]	1 [0.0]	1 [2.0]	
Thymus	(49)	(46)	(46)	(49)	
Hemorrhage	1 [2.0]	(40)	(40)	5 [2.4]	
i lemorriage	1 [2.0]			5 [2. 4]	
ITEGUMENTARY SYSTEM					
Mammary Gland	(49)	(48)	(47)	(48)	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE

CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Hyperplasia Skin Inflammation, Chronic Ulcer Cyst Epithelial Inclusion Epidermis, Hyperplasia Epidermis, Skin, Site Of Application, Hyperplasia Skin, Site Of Application, Erosion	31 [3.1] (49) 5 [3.6] 4 [3.5] 9 [3.6] 1 [1.0]	25 [2.8] (50) 1 [4.0] 5 [3.4] 4 7 [3.6] 10 [1.0]	29 [3.0] (50) 2 [4.0] 5 [4.0] 2 8 [3.5] 29 [1.1]	10 [2.7] (50) 2 [2.5] 4 [3.5] 6 [3.5] 19 [1.1]	
Skin, Site Of Application, Inflammation, Chronic		6 [1.0]	12 [1.0]	11 [1.0]	
MUSCULOSKELETAL SYSTEM Bone Cranium, Osteopetrosis Femur, Osteopetrosis	(50) 1 [2.0]	(50)	(50)	(50) 1 [3.0]	
NERVOUS SYSTEM					
Brain Compression Hydrocephalus Hemorrhage Gliosis Arteriole, Necrosis, Fibrinoid Neuron, Necrosis	(50) 16 [3.2] 7 [2.0] 1 [1.0]	(50) 10 [3.0] 1 [2.0] 1 [1.0]	(50) 15 [3.1] 5 [2.0] 3 [1.7] 1 [2.0]	(50) 4 [3.5] 2 [2.5] 11 [2.5] 2 [1.0] 5 [1.8] 16 [1.9]	
RESPIRATORY SYSTEM					
Lung Infiltration Cellular, Histiocyte Hemorrhage Inflammation, Chronic Edema Metaplasia, Osseous Alveolar Epithelium, Hyperplasia Nose	(50) 21 [1.5] 6 [1.7] 9 [1.2] 2 [2.5] 10 [1.3] (50)	(50) 19 [1.5] 6 [2.0] 13 [1.2] 2 [2.5] 2 [2.5] 4 [2.5] (50)	(50) 21 [1.3] 7 [2.1] 16 [1.4] 2 [1.5] 6 [2.0] (50)	(50) 12 [1.3] 17 [2.0] 12 [1.8] 2 [2.5] 1 [1.0] 6 [2.5] (50)	

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Route: SKIN APPLICATION

Species/Strain: RATS/F 344

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FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Foreign Body Inflammation, Chronic Respiratory Epithelium, Hyperplasia Respiratory Epithelium, Metaplasia, Squamous	13 15 [2.2] 11 [1.8] 2 [2.0]	22 22 [1.5] 11 [1.7]	12 13 [1.8] 8 [1.9]	12 11 [1.6] 9 [1.3] 1 [1.0]	
SPECIAL SENSES SYSTEM					
Eye Cataract Cornea, Hyperplasia Cornea, Inflammation, Chronic Cornea, Ulcer Retina, Degeneration Harderian Gland Inflammation, Chronic Hyperplasia, Focal	(50) 4 [1.8] (50)	(50) 1 [3.0] 1 [1.0] 1 [3.0] (50) 1 [3.0] 1 [2.0]	(50) 2 [2.0] 1 [2.0] 5 [1.8] 6 [2.0] (50) 1 [2.0]	(50) 1 [2.0] 5 [2.4] 23 [1.7] 1 [3.0] 3 [2.0] (50) 1 [2.0]	
URINARY SYSTEM					
Kidney Nephropathy Inflammation, Chronic Cyst Renal Tubule, Accumulation, Hyaline Droplet	(50) 43 [2.2] 3 [2.7]	(50) 46 [1.8] 5 [2.4] 1 [3.0]	(50) 42 [2.3] 9 [2.3]	(50) 30 [1.4] 1 [3.0] 1 [3.0]	
Renal Tubule, Dilatation Renal Tubule, Hyperplasia Renal Tubule, Necrosis Renal Tubule, Pigmentation Transitional Epithelium, Hyperplasia Urethra Angiectasis Urinary Bladder	1 [2.0] 2 [3.0] 2 [3.0] (0) (50)	1 [3.0] 4 [2.8] (0) (50)	2 [3.5] 1 [2.0] (1) 1 [4.0] (50)	1 [2.0] (0) (49)	
Hemorrhage Inflammation, Chronic Transitional Epithelium, Hyperplasia	, ,		1 [2.0] 2 [2.5] 1 [4.0]	3 [3.0] 4 [2.5]	

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Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG

*** END OF MALE ***

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

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FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG
Disposition Summary				
Animals Initially in Study Early Deaths	50	50	50	50
Moribund Sacrifice Natural Death	13 7	9 9	10 8	14 10
Survivors Terminal Sacrifice	30	32	32	25
Other Animals Examined Microscopically	50	50	50	1 49
ALIMENTARY SYSTEM				
Intestine Large, Cecum	(50)	(50)	(50)	(49)
Edema Inflammation, Chronic	1 [2.0]	3 [2.0] 1 [3.0]	1 [3.0]	2 [3.0]
Intestine Large, Rectum	(50)	(48)	(43)	(44)
Hemorrhage Intestine Small, Duodenum	(49)	(50)	(50)	1 [2.0] (49)
Epithelium, Hyperplasia	1 [1.0]			
Intestine Small, Jejunum	(47)	(50)	(50)	(46)
Epithelium, Hyperplasia Liver	(50)	(50)	1 [1.0] (50)	(49)
Basophilic Focus	42	43	45	40
Infiltration Cellular, Mixed Cell	8 [1.8]	11 [1.5]	13 <u>[</u> 1.6]	8 [1.4]
Mixed Cell Focus Hematopoietic Cell Proliferation	3	5	7	1
Necrosis, Focal	1 [1.0] 5 [1.4]	1 [1.0]	1 [1.0] 3 [1.7]	4 [1.5]
Eosinophilic Focus	4	3	8	- [1.5]
Clear Cell Focus	10	6	4	4
Hepatodiaphragmatic Nodule	11	6	12	8
Regeneration	1 [2.0]	4 [0 0]	0.10.01	2 [2.5]
Hemorrhage		1 [2.0]	2 [2.0] 1 [3.0]	1 [3.0]
Cyst Angiectasis			1 [3.0] 1 [2.0]	1 [2.0]
Bile Duct, Hyperplasia	5 [1.6]	3 [1.3]	2 [1.5]	5 [1.8]
Centrilobular, Necrosis	1 [2.0]			2 [1.5]
Hepatocyte, Vacuolization Cytoplasmic	5 [2.8]	5 [2.8]	3 [3.0]	4 [3.0]

a - Number of animals examined microscopically at site and number of animals with lesion

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Species/Strain: RATS/F 344

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FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Kupffer Cell, Pigmentation Mesentery Fat, Necrosis Oral Mucosa Cyst Pancreas Atrophy	1 [2.0] (11) 11 [2.9] (1) (50) 15 [1.5]	1 [2.0] (12) 11 [2.7] (0) (50) 16 [2.1]	(9) 8 [3.0] (2) 1 [3.0] (50) 18 [1.8]	1 [2.0] (9) 9 [2.7] (0) (49) 19 [2.1]	
Cyst Necrosis Acinus, Cytoplasmic Alteration Acinus, Hyperplasia, Focal Salivary Glands Atrophy Stomach, Forestomach Ulcer Edema Epithelium, Hyperplasia Stomach, Glandular Erosion Ulcer Edema Glands, Hyperplasia	4 [3.0] (50) 3 [2.0] (50) 3 [3.7] 2 [2.5] 4 [2.5] (50) 1 [3.0]	6 [3.0] 1 [3.0] 1 [2.0] (50) 1 [3.0] (50) (50) 1 [3.0] 1 [2.0]	5 [3.0] 1 [3.0] 1 [2.0] (50) 1 [3.0] (50) 1 [4.0] 1 [3.0] 2 [2.5] (50) 2 [3.0] 1 [2.0] 1 [3.0] 1 [3.0]	1 [3.0] (48) 1 [2.0] (49) 4 [3.5] 2 [2.5] 2 [2.5] (49) 4 [2.3] 1 [2.0] 1 [3.0]	
CARDIOVASCULAR SYSTEM Heart Cardiomyopathy Thrombosis Inflammation, Chronic	(50) 30 [1.5] 1 [4.0]	(50) 39 [1.8] 1 [4.0] 1 [3.0]	(50) 35 [1.9] 1 [3.0]	(49) 31 [1.5] 1 [3.0] 1 [3.0]	
ENDOCRINE SYSTEM Adrenal Cortex Degeneration, Fatty Hyperplasia, Focal Hypertrophy, Focal Accessory Adrenal Cortical Nodule Adrenal Medulla Hyperplasia	(50) 20 [2.1] 3 [1.7] 10 [2.3] 9 [3.0] (49) 5 [1.2]	(50) 15 [2.5] 10 [2.2] 6 [3.0] (50) 2 [1.0]	(50) 16 [2.5] 4 [2.3] 9 [1.8] 9 [3.0] (50) 4 [2.0]	(49) 17 [2.1] 5 [1.0] 8 [2.4] 8 [3.0] (49) 2 [1.0]	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE

CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

Time Report Regsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Islets, Pancreatic	(50)	(50)	(50)	(49)	
Hyperplasia	1 [2.0]	(/	2 [2.0]	(- /	
Metaplasia, Hepatocyte		1 [2.0]			
Pituitary Gland	(50)	(50)	(50)	(49)	
Pars Distalis, Angiectasis	1 [2.0]	6 [2.5]	4 [2.8]	4 [3.5]	
Pars Distalis, Cyst	16 [3.0]	6 [3.0]	15 [3.0]	14 [3.0]	
Pars Distalis, Hyperplasia, Focal	7 [2.3]	7 [2.0]	10 [2.4]	11 [2.2]	
Pars Intermedia, Angiectasis		1 [2.0]	2 [3.0]	2 [2.5]	
Pars Intermedia, Cyst	1 [3.0]	1 [3.0]	2 [3.0]		
Thyroid Gland	(50)	(50)	(50)	(49)	
Últimobranchial Cyst				2 [3.0]	
C-cell, Hyperplasia	17 [1.6]	14 [1.5]	10 [1.8]	12 [1.6]	
Follicle, Cyst	2 [3.0]	2 [3.0]	3 [3.0]	1 [3.0]	
Follicular Cell, Hyperplasia	1 [1.0]		1 [1.0]	1 [2.0]	
ENERAL BODY SYSTEM None					
None ENITAL SYSTEM	(50)	(49)	(50)	(49)	
None ENITAL SYSTEM Clitoral Gland	(50) 13 [2 3]	(49) 2 [2 0]	(50) 10 [2 3]	(49) 3 [2 0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic	13 [2.3]	2 [2.0]	10 [2.3]	3 [2.0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst		2 [2.0] 3 [3.0]	10 [2.3] 1 [3.0]		
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia	13 [2.3] 1 [3.0]	2 [2.0] 3 [3.0] 2 [2.0]	10 [2.3] 1 [3.0] 2 [1.0]	3 [2.0] 3 [3.0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary	13 [2.3] 1 [3.0] (50)	2 [2.0] 3 [3.0] 2 [2.0] (50)	10 [2.3] 1 [3.0] 2 [1.0] (50)	3 [2.0] 3 [3.0] (49)	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst	13 [2.3] 1 [3.0] (50) 11 [3.0]	2 [2.0] 3 [3.0] 2 [2.0]	10 [2.3] 1 [3.0] 2 [1.0]	3 [2.0] 3 [3.0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst Angiectasis	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0]	2 [2.0] 3 [3.0] 2 [2.0] (50)	10 [2.3] 1 [3.0] 2 [1.0] (50)	3 [2.0] 3 [3.0] (49)	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0] 1 [3.0]	2 [2.0] 3 [3.0] 2 [2.0] (50) 8 [3.0]	10 [2.3] 1 [3.0] 2 [1.0] (50) 9 [3.0]	3 [2.0] 3 [3.0] (49) 6 [3.0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst Angiectasis Corpus Luteum, Hyperplasia	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0] 1 [3.0] (50)	2 [2.0] 3 [3.0] 2 [2.0] (50) 8 [3.0]	10 [2.3] 1 [3.0] 2 [1.0] (50) 9 [3.0]	3 [2.0] 3 [3.0] (49) 6 [3.0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst Angiectasis Corpus Luteum, Hyperplasia Uterus	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0] 1 [3.0]	2 [2.0] 3 [3.0] 2 [2.0] (50) 8 [3.0] (50) 10 [2.2]	10 [2.3] 1 [3.0] 2 [1.0] (50) 9 [3.0] (50) 5 [2.2]	3 [2.0] 3 [3.0] (49) 6 [3.0] (49) 9 [2.4]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst Angiectasis Corpus Luteum, Hyperplasia Uterus Endometrium, Hyperplasia, Cystic Vagina	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0] 1 [3.0] (50) 4 [2.8] (6)	2 [2.0] 3 [3.0] 2 [2.0] (50) 8 [3.0]	10 [2.3] 1 [3.0] 2 [1.0] (50) 9 [3.0]	3 [2.0] 3 [3.0] (49) 6 [3.0]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst Angiectasis Corpus Luteum, Hyperplasia Uterus Endometrium, Hyperplasia, Cystic	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0] 1 [3.0] (50) 4 [2.8]	2 [2.0] 3 [3.0] 2 [2.0] (50) 8 [3.0] (50) 10 [2.2]	10 [2.3] 1 [3.0] 2 [1.0] (50) 9 [3.0] (50) 5 [2.2]	3 [2.0] 3 [3.0] (49) 6 [3.0] (49) 9 [2.4]	
None ENITAL SYSTEM Clitoral Gland Inflammation, Chronic Cyst Hyperplasia Ovary Cyst Angiectasis Corpus Luteum, Hyperplasia Uterus Endometrium, Hyperplasia, Cystic Vagina Inflammation, Chronic	13 [2.3] 1 [3.0] (50) 11 [3.0] 1 [4.0] 1 [3.0] (50) 4 [2.8] (6) 1 [4.0]	2 [2.0] 3 [3.0] 2 [2.0] (50) 8 [3.0] (50) 10 [2.2] (6)	10 [2.3] 1 [3.0] 2 [1.0] (50) 9 [3.0] (50) 5 [2.2]	3 [2.0] 3 [3.0] (49) 6 [3.0] (49) 9 [2.4]	

a - Number of animals examined microscopically at site and number of animals with lesion b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Hyperplasia	6 [3.2]	8 [2.6]	3 [2.7]	6 [2.7]	
Myelofibrosis		1 [2.0]	2 [3.0]	2 [2.0]	
Infiltration Cellular, Histiocyte Lymph Node	(13)	(10)	(14)	2 [3.0] (8)	
Deep Cervical, Hemorrhage	(13)	1 [4.0]	(14)	(0)	
Deep Cervical, Hyperplasia, Lymphoid		1 [2.0]			
Deep Cervical, Pigmentation		1 [2.0]			
Mediastinal, Ectasia		. [=.0]	1 [2.0]		
Mediastinal, Hemorrhage	4 [1.8]	4 [3.0]	4 [1.8]	3 [2.0]	
Mediastinal, Hyperplasia, Lymphoid	3 [2.0]	5 [3.0]	7 [2.4]		
Mediastinal, Pigmentation	6 [2.7]	6 [2.7]	9 [2.8]	2 [2.5]	
Pancreatic, Hemorrhage	1 [1.0]	3 [2.0]	1 [2.0]	1 [2.0]	
Pancreatic, Hyperplasia, Lymphoid		1 [2.0]			
Pancreatic, Pigmentation	1 [2.0]	2 [2.5]	1 [3.0]	1 [3.0]	
Lymph Node, Mandibular	(3)	(7)	(1)	(2)	
Ectasia	1 [2.0]	4 [2.5]		1 [2.0]	
Hyperplasia, Lymphoid	1 [2.0]	4 [0 0]			
Pigmentation Lymph Node, Mesenteric	1 [2.0] (50)	1 [2.0] (50)	(50)	(40)	
Pigmentation	25 [2.1]	24 [2.1]	27 [2.0]	(48) 17 [2.0]	
Hemorrhage	11 [1.5]	11 [1.1]	6 [1.5]	5 [1.8]	
Hyperplasia, Lymphoid	16 [2.3]	20 [2.3]	12 [2.1]	11 [2.3]	
Ectasia	10 [2.0]	1 [3.0]	12 [2.1]	1 [3.0]	
Necrosis		. [0.0]		1 [3.0]	
Spleen	(50)	(50)	(50)	(49)	
Pigmentation	10 [3.0]	16 [3.1]	13 [3.1]	16 [3.0]	
Hematopoietic Cell Proliferation	21 [2.0]	29 [1.7]	29 [1.7]	20 [1.8]	
Necrosis	1 [3.0]	1 [3.0]	2 [4.0]		
Fibrosis		1 [2.0]		2 [3.0]	
Hemorrhage				2 [3.0]	
Hyperplasia, Reticulum Cell		0.10.01		1 [3.0]	
Lymphoid Follicle, Atrophy	4 [0 0]	2 [3.0]	0.10.01	1 [3.0]	
Lymphoid Follicle, Hyperplasia	1 [3.0]	(40)	3 [3.3]	1 [3.0]	
Thymus Hyperplasia, Lymphoid	(50) 1 [3.0]	(48) 2 [2.5]	(49) 1 [3.0]	(46) 1 [2.0]	
Hemorrhage	1 [3.0] 2 [1.5]	2 [2.5] 2 [2.0]	1 [3.0] 1 [2.0]	1 [2.0] 1 [3.0]	

INTEGUMENTARY SYSTEM

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE

CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005

Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Mammary Gland Hyperplasia Skin	(50) 45 [3.0] (50)	(50) 46 [2.9] (50)	(50) 45 [2.9] (50)	(48) 41 [2.7] (49)	
Inflammation, Chronic Cyst Epithelial Inclusion Ulcer	2 [3.5]	1 [1.0] 1	1 [4.0]	(10)	
Epidermis, Skin, Site Of Application, Hyperplasia	1 [1.0]	5 [1.0]	16 [1.0]	21 [1.0]	
Epidermis, Hyperplasia Skin, Site Of Application, Inflammation, Chronic	2 [3.5]	2 [1.5]	2 [2.5] 3 [1.0]	1 [2.0] 10 [1.0]	
MUSCULOSKELETAL SYSTEM					
None					
NERVOUS SYSTEM					
Brain Compression Hydrocephalus Necrosis Gliosis Hemorrhage Angiectasis	(50) 14 [2.9] 2 [2.5] 2 [2.5] 1 [3.0] 1 [1.0] 1 [3.0]	(50) 13 [3.7] 8 [2.3] 1 [2.0] 1 [3.0] 8 [1.4]	(50) 14 [3.3] 1 [2.0] 2 [2.5] 2 [2.5] 1 [2.0]	(49) 13 [3.1] 2 [2.0]	
RESPIRATORY SYSTEM					
Lung Inflammation, Chronic Infiltration Cellular, Histiocyte Hemorrhage Metaplasia, Squamous Edema Metaplasia, Osseous Emphysema	(50) 10 [1.9] 22 [1.2] 8 [1.6] 1 [3.0] 4 [2.0]	(50) 22 [1.5] 26 [1.2] 14 [1.9] 4 [2.8]	(50) 19 [1.5] 30 [1.5] 9 [1.8] 1 [2.0] 3 [3.0] 2 [1.0] 1 [4.0]	(49) 10 [1.1] 27 [1.2] 13 [1.8] 2 [2.5] 1 [1.0]	
Pigmentation Alveolar Epithelium, Hyperplasia	3 [1.3]	4 [2.3]	10 [1.9]	1 [2.0] 1 [1.0]	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Route: SKIN APPLICATION

Species/Strain: RATS/F 344

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

DIISOPROPYLCARBODIIMIDE CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Regsted: 08/08/2005

Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG
Nose	(50)	(50)	(50)	(49)
Foreign Body	5	4.54.01	2	3
Inflammation, Chronic Respiratory Epithelium, Hyperplasia	6 [1.7] 4 [1.8]	1 [1.0] 1 [1.0]	2 [1.5] 2 [1.5]	3 [2.3] 1 [2.0]
SPECIAL SENSES SYSTEM				
Eye	(50)	(50)	(50)	(49)
Cataract	2 [3.0]	5 [2.6]	3 [3.0]	3 [2.3]
Cornea, Hyperplasia				3 [1.7]
Cornea, Inflammation, Chronic	1 [1.0]	1 [4.0]		3 [1.3]
Retina, Degeneration	4 [3.0]	7 [3.0]	5 [2.8]	4 [2.5]
Retina, Dysplasia		.	1 [1.0]	4
Harderian Gland	(50)	(50)	(50)	(49)
Hyperplasia, Focal Inflammation, Chronic	1 [1.0]	1 [4.0]		
JRINARY SYSTEM		. [0]		
Kidney	(50)	(50)	(50)	(49)
Nephropathy	32 [2.1]	32 [1.6]	28 [2.0]	21 [1.7]
Inflammation, Suppurative	1 [4.0]	02 [1.0]	20 [2.0]	2.[]
Cyst	1 [3.0]			
Inflammation, Chronic	2 [2.0]	2 [2.0]	1 [2.0]	
Infarct	1 [1.0]		1 [3.0]	
Hemorrhage				1 [3.0]
Papilla, Necrosis				1 [4.0]
Renal Tubule, Accumulation, Hyaline	2 [2.5]	1 [4.0]		2 [2.5]
Droplet Renal Tubule, Dilatation	1 [2 0]		1 [2 0]	1 [2 0]
Renal Tubule, Dilatation Renal Tubule, Necrosis	1 [2.0] 1 [2.0]	2 [2.0]	1 [2.0]	1 [2.0] 2 [2.5]
Transitional Epithelium, Hyperplasia	۱ [۲.۵]	ک زک.ن	1 [3.0]	ک زکان
Urinary Bladder	(50)	(50)	(50)	(49)
Hemorrhage	(00)	(00)	1 [3.0]	()

*** END OF REPORT ***

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)